

Topical Hydrocortisone From Prescription to Over-the-Counter Sale

A Past Controversy: A Cautionary Tale

IT HAS BEEN 25 YEARS SINCE topical hydrocortisone was approved for over-the-counter (OTC) sale to the public and 40 years since the American Academy of Dermatology's first committee to evaluate the proposal rejected OTC hydrocortisone being as too risky and hazardous for the public. Whenever a regulatory issue related to dermatology is likely to have an impact on the public at large, the need for organized dermatology to adopt a position, the mechanisms of so doing, and the likelihood of the position being proven correct over time remain the same. With that in mind, we review an issue that generated considerable controversy in its time and on which, in hindsight, organized dermatology proved to be on the wrong side.

Topical hydrocortisone cream was first found to be an effective therapy in 1952 when Sulzberger and Witten¹ used it to treat eczematous dermatitis. Since then, multiple formulations have been developed with varying potencies. In the United States, from 1952 to 1979, hydrocortisone was available only with a prescription. In 1965 and again in 1975, the American Academy of Dermatology appointed committees to evaluate the safety of OTC use of hydrocortisone. On both occasions, the committees concluded that the risk for abuse and hazards to the public were too great to recommend approval. The controversy continued until 1979, when a US Food and Drug Administration (FDA) subcommittee approved it for OTC use. At that time, 0.5% hydrocortisone cream became available in the United States. In the 2 years following the change, it was estimated that the US public saved ap-

proximately \$600 million as a result.² In 1991, the current 1% formulation of hydrocortisone cream was approved.³ This article discusses the opinions of leading dermatologists regarding the transfer of hydrocortisone to OTC status in the United States and England and reviews the literature for evidence of adverse effects from the use of hydrocortisone after it became available OTC.

During the 1950s through the 1970s, many dermatologists were opposed to having hydrocortisone available as an OTC agent. In 1977, the American Academy of Dermatology conducted a survey of its members that documented a strong resistance to the change to OTC status. Opponents were concerned about the potential for inappropriate application of hydrocortisone cream by consumers. They feared misuse would mask the development and delay the diagnosis of skin cancers or other skin conditions. Critics were also concerned about the adverse effects of hydrocortisone cream, such as atrophy, striae, and steroid-induced rosacea.

Peyton Weary, MD, a dermatologist, expressed his reservations in a correspondence in the *Journal of the American Academy of Dermatology*.⁴ Weary feared that the change would lead to the improper use of hydrocortisone by "quasi skin care providers,"^{4(p454)} such as cosmetologists, beauticians, and barbers. He believed that the potential adverse effects of topical hydrocortisone cream posed a major risk to the general public. Because of this, he suggested the necessity for a swift implementation of a postmarketing surveillance system if this medication were to be approved. He labeled the switch to OTC a "misadventure."^{4(p454)} (The withdrawal of

Vioxx from the market recently highlighted the need for better post-marketing surveillance, a process which in some countries is done by an agency separate from that which approves drugs for marketing.)

Lawrence Solomon, MD, a dermatologist and a member of the FDA subcommittee that approved the OTC sale of hydrocortisone cream, criticized Weary's apprehension regarding the change to OTC.⁵ He believed hydrocortisone posed less of a threat to the public than other already accessible OTC products, such as benzocaine, salicylic acid, and tars. Solomon maintained that the adverse reactions reported by Weary are the effects of topical steroids in general and are not specific to the formulation of 0.5% hydrocortisone cream. He also felt that this guilt-by-association scheme provided by Weary was invalid, despite testimony that Weary provided in his reply.⁵ Furthermore, Solomon stressed the need to limit the government's control over patient access to what he believed to be a benign medication, in light of the FDA's findings that hydrocortisone was a rather harmless agent.

E. William Rosenberg, MD, a dermatologist who wrote a companion article⁶ to that of Weary, expressed his belief that hydrocortisone cream should be available without a prescription. Rosenberg emphasized that hydrocortisone was a safe medication even if used inappropriately.⁷ He opined that there would be minimal risk to the public with proper labeling. Moreover, he felt confident that the consumer had the ability to recognize the appropriate circumstances to apply topical hydrocortisone. In that instance, he believed that if topical hydrocortisone were available, patients would be less likely to

use more dangerous or irritating products in the self-treatment of skin diseases that did not respond to other topical therapies. Thus, Rosenberg felt that patients were capable of self-diagnosing trivial dermatoses.

A similar debate occurred in other countries. Sam Shuster, MD, PhD, of the Royal Victoria Infirmary, Newcastle upon Tyne, England, was opposed to the change of topical hydrocortisone to an OTC status in England.⁸ His main concern was that the adverse effects of topical hydrocortisone are too dangerous and could lead to Cushing syndrome. He based this opinion on a study in which 1% hydrocortisone applied to a rat resulted in a reduction of glucocorticoid cytosol receptors in the skin by 70% to 80%; on normal human skin, this same composition of hydrocortisone cream led to vasoconstriction. Based on these results, Shuster opined that systemic absorption could occur after topical application. He was concerned about the potential ability of hydrocortisone to produce skin atrophy, perioral dermatitis, and a reduction in the skin's natural resistance to infection.

Malcolm Greaves, MD, PhD, of the Institute of Dermatology at the University of London, London, England, directly responded to Shuster's letter.⁹ In his response, Greaves pointed out that there is little evidence to support the contention that the topical use of 0.5% hydrocortisone cream could lead to the adverse effects discussed by Shuster. However, Greaves conceded that hydrocortisone is not without its minor harmful reactions. He highlighted a case report of local atrophy after prolonged use of 1% hydrocortisone cream over the eyelid.¹⁰ This same article described 3 patients who developed rosacea-like eruptions after using topical hydrocortisone for 1 to 3 months. However, Greaves did not find any evidence to substantiate Shuster's claim that topical hydrocortisone reduces the resistance to infection by bacteria and fungus. Furthermore, he believed that self-application of hydrocortisone cream was a justifiable and safe approach after exposure to an irritating substance. He could not comprehend how people

could criticize the use of hydrocortisone cream for the treatment of rash of unknown etiology when patients readily use analgesic and anti-inflammatory OTC agents for headaches and joint pains without understanding their causes. Greaves also referred to a symposium on self-medication that indicated that 60% of patients who use a medication for a skin problem obtain it without seeking medical advice. This study confirmed his belief that without the availability of hydrocortisone, patients would use harsher, more dangerous topical therapies for their skin ailments.

Many supporters of the switch to OTC status in England based their endorsement on the success seen in the United States and the Scandinavian countries. Anthony Du Vivier, MD, a dermatologist at King's College Hospital, London, agreed that hydrocortisone should be available OTC.¹¹ He rested his support partially on the fact that hydrocortisone had been available OTC in the Scandinavian countries since the 1950s without generating literature on its adverse effects. Rather, the only criticism of its use had been its lack of effectiveness. Drawing on his personal experience, Du Vivier concluded that topical hydrocortisone is safe for OTC use because he had never witnessed a case of its application causing Cushing syndrome. He was alarmed by Shuster's claim that use of 1% hydrocortisone cream on normal skin could cause Cushing syndrome. On the contrary, he believed it to be a weak steroid incapable of producing such dramatic effects. In addition, Du Vivier emphasized the need to include package inserts detailing the proper and improper indications for hydrocortisone application.

On review of the literature detailing the adverse effects of hydrocortisone, as well as the debate surrounding its approval for OTC distribution, it is clear that the change in status was reasonable. This is evidenced by the fact that over the past 30 years, only a handful of reports have been published regarding its adverse effects. However, it is important to note that this scarcity could be due to the lack of reporting by both physicians and patients.

We found 3 articles that illustrate adverse effects of topical hydrocortisone after its change to OTC status. One article documented hydrocortisone-induced rosacea in prepubertal children.¹² These findings were surprising because before this study, it was presumed that this low-strength topical steroid was safe for use in children. The authors determined that these patients might have had a genetic predisposition to developing steroid-induced rosacea. The second article, which has already been mentioned, consists of several case reports of complications from topical hydrocortisone.¹⁰ It specifically details 3 case reports of steroid-induced rosacea after hydrocortisone use, 1 case of perioral dermatitis, as well as a case of atrophy and telangiectasia of the eyelids after prolonged use. The third article describes the use of OTC steroid creams as a potential cause of immunosuppression in homosexual individuals.¹³ The author of this article believes that there could be a link between the use of available OTC steroid creams and the upsurge in reports of overwhelming infections in immunodeficient homosexual patients. This possible link was evidence enough for the authors to suggest warnings to be issued to men and women against the use of OTC creams and ointments in the anogenital region. The results of these reports do show that physicians should still be concerned about patients who self-treat, especially about treating children on sensitive areas (ie, the face or groin) for prolonged periods of time and immunodeficient patients in the anogenital regions.

Without a body of knowledge currently available to the medical community, it seems apparent that the switch to OTC status was a boon rather than a misadventure. In fact, when initially approved for OTC status in 1979, topical hydrocortisone was available in a 0.5% formulation. Twelve years later, based on extensive safety and effectiveness data, the FDA permitted the OTC sale of products containing up to 1% hydrocortisone.³ Nonprescription medications account for about 60% of all medications used in the United States and may be used to treat or

cure 400 ailments. Thirty percent of OTC drugs marketed between 1975 and 1994 were products that had been changed from prescription to OTC.¹⁴ From this, it is obvious that despite opposition by organized dermatology groups and many of our opinion leaders, the FDA acted in the best interests of the patient and approved a safe topical cream for the treatment of minor skin inflammation and pruritus. This regulatory episode may serve to remind us to be circumspect regarding our ability to predict the effects of changes in drug regulation or of other public policies. Although there is no way to be certain that the view of organized dermatology will not be out of step, inclusion of members of related specialties and/or the public on the committees that develop our policies on national issues may help us avoid policies that are too narrow to be correct.

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Accepted for Publication: November 12, 2006.

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Author Contributions: Dr Ravis had full access to all of the data in the study and takes responsibility for the integrity of the data and the accu-

racy of the data analysis. *Study concept and design:* Ravis and Eaglstein. *Acquisition of data:* Ravis and Eaglstein. *Analysis and interpretation of data:* Ravis and Eaglstein. *Drafting of the manuscript:* Ravis and Eaglstein. *Critical revision of the manuscript for important intellectual content:* Ravis and Eaglstein. *Administrative, technical, or material support:* Ravis and Eaglstein. *Study supervision:* Ravis and Eaglstein.

Financial Disclosure: Dr Eaglstein is employed by Stiefel Laboratories Inc as Vice President of Pipeline Development and Scientific Affairs. During the preparation of this article Dr Eaglstein was employed by Ivax Corporation and Teva Pharmaceuticals Inc as President of Ivax Dermatologicals. He was a consultant for Photopharmica and Closure Medical Inc. He owns stock options in Teva Pharmaceuticals Inc and stock in Merck & Co Inc, Dusa Pharmaceuticals, ISIS Pharmaceuticals, Pfizer, Connetics, Smith & Nephew, QLT Inc, and ViroPharma. Neither Ivax (Teva) nor Stiefel Laboratories had a role in the design and conduct, collection, management, analysis, preparation review, or approval of any other role in this manuscript.

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